REMARKS

The examiner's reconsideration of the application is requested in view of the amendments above and comments which follow.

Claim 12 is rejected under 35 U.S.C. §112 for failing to define X_2. This rejection is not understood because there is no pending claim 12 (this claim was cancelled without prejudice with the Amendment dated December 7, 2001) and because in pending claims 43 and 45, X_2 is clearly defined.

Claim 50 has also been rejected under 35 U.S.C. §112 as being indefinite. Clarification is accomplished by replacing '' provided that '' with '' and wherein '' in the terminal part of claim 50.

Claim 52 is objected to as dependent upon a rejected base claim. This objection is now resolved by the amendment consisting in rewriting claim 52 as an independent claim. Since no other objection or rejection was made with respect to claim 52, amended claim 52 is now allowable. New claim 58 dependent upon claim 52 has been filed in order to specify the nature of the functional end group, which should be allowable for the same reason.

In order to more particularly point out and distinctly claim the subject matter which applicant regards as the invention, claim 37 is cancelled and claims 36, 44-46, 48-50, 53, 55 and 57 are amended as explained below. Claims 38-43, 47, 51, 54 and 56 are not amended.

Claim 36 is amended by inserting therein the features of claim 37 and further replacing ''amine, carboxyl '' with '' functionalized amines, N-acyl '', the amendments having support at page 19 lines 7-17 of the specification as originally filed.

Claims 46, 48, 50, 53, 55 and 57 are amended in the same manner as claim 36 with respect to the poly-α-aminoacid derivative involved therein. Claim 46 is further amended by more clearly reciting the step feature which renders the process novel and unobvious.

Claims 44, 45 and 49 are amended by introducing the definition of m, said amendment having support at page 9 line 24 of the specification as originally filed.

Claims 36-49 and 51 are rejected under 35 U.S.C. 102(b) as being anticipated by British Patent No. 781,202. Reconsideration is requested.

British Patent No. 781,202 teaches polymerizing the anhydrocarboxyamino-acid of γ-benzyl-L-glutamate or γ-methyl-L-glutamate in the presence of a catalyst such as a tertiary base or a primary amine or pentamethyl guanidine (page 1 col. 2, lines 43-52 and 57-60). The result of the catalyst in such polymerisation is merely to promote rapid polymerization of the monomer (page 1, col. 2 lines 54-56), not to introduce chemical functionality into the polymer.

The present invention deals with introducing chemical functionality at one or more ends of a polymer having glutamic or aspartic or serinic repeating units in the backbone. This is achieved, e.g. according to the process of claim 46, by effecting polymerization of an amino-acid N-carboxy anhydride in the presence of a multifunctional initiator containing the desired functionality or a bifunctional terminating agent. The result of the invention necessarily distinguishes over the result of British Patent No. 781,202 by the presence of functional end group(s) onto the polymer. Moreover, nothing in the identified prior art would motivate the skilled person to make a functional derivative of the polymer disclosed in British Patent No. 781,202. Therefore, the subject matter of claims 36-49 and 51 is not obvious in view of British Patent No. 781,202.

Claims 50, 53 and 54 are rejected under 35 U.S.C. §102(b) as being anticipated by DE MARRE et al. The Examiner indicates that the subject matter of these claims is not new because DE MARRE ET AL. discloses a polyglutamine suitable as a carrier for macromolecular drugs. The applicant respectfully disagrees for the following reasons:

DE MARRE ET AL. discloses polymers of N-(2-hydroxyethyl)-L-glutamine (hereinafter referred as PHEG for convenience). However claims 50, 53 and 54 do not refer to PHEG in general, but to modified derivatives thereof having specific functional groups at one or both ends of the polymer backbone, and DE MARRE ET AL. does not disclose any type of PHEG in general but only specific variants thereof.

More specifically, DE MARRE ET AL. discloses partial conversion of hydroxyl side groups of PHEG into reactive carbonate esters (i.e. oxycarbonyl groups) through PHEG reaction with 4-nitrophenyl chloroformate. This teaching is an unambiguous confirmation that functionalization occurs on the pending side chains of PHEG. DE MARRE ET AL. further discloses that during said conversion, no intra- or intermolecular carbonate esters are formed, and that the carbonate ester formed easily reacts with numerous amines. Thus DE MARRE ET AL. fails to disclose any functionality at one or more terminal ends of the polymer backbone. There is no teaching in DE MARRE ET AL., and no motivation from DE MARRE ET AL., of introducing into PHEG the specific functional end groups which are recited by claims 50, 53 and 54.

Claims 38-51 and 53-57 are rejected under 35 U.S.C. §102(b) as being anticipated by International Patent Publication WO 98/19710 (SCHACHT et al.). The applicant respectfully disagrees for the following reason: the most relevant portions of SCHACHT ET AL. are to be

found in example 1 (pages 15 and 18), example 8 (page 27), example 12 (page 41), example 13.2 (page 43), example 15 (page 45) and example 17 (page 50).

SCHACHT ET AL. generally discloses (page 6 lines 25-30) a reactive hydrophilic polymer including activated esters, thiol groups, biotin or aldehyde groups which may be carried by side chains of the main polymer backbone and, more specifically, aldehyde groups incorporated in PHEG.

Example 1 discloses a polymeric precursor obtained by copolymerizing N-2-hydroxypropyl-methacrylamide with the 4-nitrophenyl ester of a *N*-methacryloylated peptide wherein the terminal p-nitrophenoxy groups of the peptide side chains are suitable for subsequent addition reactions. The same teaching is repeated in example 8 and the monomeric structures shown at page 28.

Examples 12 (page 41 lines 12-30), 13.2 (page 43 lines 16-28) and 15 (page 45 lines 1-21) all disclose first preparing a 4-nitrophenyl chloroformate activated PHEG, wherein the p-nitrophenoxy groups are later converted by subsequent addition reactions. Figures 6B, 7B and 9 illustrate these reactions and make it clear that all functional groups are on the pending side chains, which is also confirmed by the title of example 15 ('' ... side chains '').

Thus in all the closest embodiments of SCHACHT ET AL., it is clear that the reactive groups are side groups of the polyglutamic acid derivative which can form (page 6 lines 20-24) a plurality of cross-linkages with a nucleic acid-containing cationic polyelectrolyte.

In summary, there is no disclosure in SCHACHT ET AL. of a poly-α-amino-acid derivative having the repeating units and having the polymer backbone terminal functional group(s)

unit derived from glutamic acid, aspartic acid or serine by means of an effective amount of an amino-alcohol, in the presence of an effective amount of a reaction promoter.

48. (currently amended) A process for making a linear monofunctional or multifunctional poly-α-amino-acid derivative having at least glutamic or aspartic or serinic repeating units in the polymer backbone and additionally having a functional group at one or both ends of the polymer backbone, the said functional end group(s) being ~~other than alcohol~~ selected from the group consisting of functionalized amines, N-acyl, ester, carbonate, thiol, thiol precursor, thioisocyanate, thiocarbonate, urea, thiourea, aldehyde, acetal, N-carboxyanhydride, oxycarbonyl, maleimide and any vinyl group suitable for radical, anionic or cationic polymerization, said process including:

- a first step of N-acylating part of an α-amino-acid selected from the group consisting of glutamic acid, aspartic acid and serine, then separately treating the N-acylated α-amino-acid and the remaining part of the said α-amino-acid in order to form a mixture of the corresponding N-carboxy anhydrides, and
- a second step of copolymerizing the said mixture of N-carboxy anhydrides in the presence of an initiator.

49. (currently amended) A process according to claim 48, wherein the N-carboxy anhydride terminated polymer obtained in the second step is reacted with a reagent having the formula $H_2N - R_3 - Y_2$, wherein:

required in claims 38-51 and 53-57. Not only cannot the skilled person arrive at the subject matter of claims 38-51 and 53-57 starting from SCHACHT ET AL., but the skilled person does not find in SCHACHT ET AL. any motivation to alter the terminal groups of the polymer backbone. This goes contrary to the teaching of the present invention wherein, as shown for instance in the reaction schemes of steps (a) and (b) at page 17 of the application and as extensively illustrated by examples 2-9, the side chain group R is kept constant while the polymer backbone amino or carboxylic acid end groups are functionalized in various ways.

Therefore, the subject matter of claims 38-51 and 53-57 is clearly unobvious with respect to SCHACHT ET AL. or a combination thereof with DE MARRE ET AL.

Given the above, it is submitted that this application is now in condition for allowance. The examiner's further and favorable reconsideration in that regard is urged.

Respectfully submitted,

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William M. Lee, Jr.
Registration No. 26,935

Barnes & Thornburg LLP
PO Box 2786
Chicago IL 60690-2786
(312) 357-1313 Telephone
(312) 759-5646 Facsimile
(312) 214-4811 Direct